IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

MAURER et al.

Serial Number: 09/147,036 Examiner: Ryan, V.

Filed: December 15, 1998 Group Art Unit: 1641

For: EXPORT SYSTEMS FOR RECOMBINANT PROTEINS

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
U.S. Patent and Trademark Office
Washington, D.C. 20231

May 15, 2000

Sir:

This is a response to the Restriction Requirement dated March 20, 2000. Applicants note that the Examiner considered the wrong set of claims for the restriction requirement. The restriction requirement is for claims 1-40 presented as the PCT application was originally filed on July 6, 1998. However, during the prosecution of the PCT application, claims 20-40 were replaced with new claims 20-38 (the original claims 21 and 23 were deleted). When the PCT application entered the national stage on September 15, 1998 in the United States, a copy of the new claims 20 to 38 was filed as pages 45-48 of the specification as evidenced by the Transmittal Sheet dated September 15, 1998 for filing an application under 35 U.S.C. 371. Applicants request that the original claims 1-19 and the new claims 20 to 38 be examined in this 371 application.

Applicants provisionally elect with traverse to prosecute Group I, claims 1-19 and 23 (new claim 23 corresponds to the original claim 25) and 34-38 (new claims 34-39 correspond to the original claims 36-40).

In response to the election of species requirement, applicants elect with traverse the transporter domain of the AIDA protein of E.coli (species A, claims 3, 20 and 38) and the passenger protein of the new claim 22 (i.e. the original claim 24), where the passenger protein present in the fusion protein "is a peptide or polypeptide having an affinity for a binding partner, or is a ligand, a receptor, an antigen, a toxin-binding protein, a protein with enzymatic activity", etc.

Applicants traverse the restriction requirement because Group II is part of the same inventive concept as Group I, especially since in the new claim 20 the transporter domain of the autotransporter is specified as the AIDA protein from E. coli. Similarly, new claim 34 now states that the AIDA protein is encoded by the vector.

Additionally, applicants traverse the restriction requirement because the inventive concept linking the two sets of claims of Groups I and II is not taught by Francisco et al. (W093/10214).

An important feature of the present invention is that the process for the presentation of peptides on the surface of gram-negative host bacteria entails the use of an autotransporter. Such an autotransporter is fused to the passenger which can actually move through it as through a pore. W093/10214 does not use or mention autotransporters but tripartite fusion proteins which include e.g. the well-known OmpA polypeptide fused to Lpp. These transmembrane proteins do not form a pore, but

instead translocation is believed to occur by membrane rearrangement. This theory has been known for some time (Georgiou et al., Protein Eng. vol. 9, pp. 239-247, 1996). Thus, the mechanism of presentation of the peptides on the surface of gram-negative host bacteria in the present invention is quite different from the mechanism taught by Francisco et al.

Another difference between the present invention and the teachings of Francisco et al is that the system of the present invention uses only two components for the fusion protein, i.e. an autotransporter and a passenger, whereas in W093/10214 three different domains are fused together. Fusing three different domains has the disadvantage that correct folding of the fusion protein cannot be ensured.

Furthermore, applicants note that, in Francisco et al., the passenger is bound via its N-terminus, whereas the passenger of the present invention is bound via its C-terminus.

Another feature of the present invention is that the peptides presented on the surface of the bacterium can be cleaved off via a protease recognition site. In contrast, the fusion proteins of Francesco et al are not designed to be cleaved.

With the above differences between the claimed invention and the teachings of Francisco et al, applicants submit that the claimed invention is a contribution over the prior art. Thus, the claims of Groups I and II belong to the same general inventive concept by sharing the same or corresponding special technical feature. As a result, the claims of Groups I and II have unity of invention. The lack of unity of invention holding should be withdrawn.

Applicants also request that the new claim 30 (the original claim 32) be joined with the elected Group I for examination on the merits. The new claim 30 is directed to a process characterized in that the modification is a proteolysis. The term "polypeptide" as mentioned in claim 22 would cover polypeptides that have been modified by proteolysis.

In the event that this paper is not timely filed, applicants petition for an appropriate extension of time. If any fees are required for the filing of this paper, please charge the fees to counsel's Deposit Account No. 01-2300.

Respectfully submitted,

Arent Fox Kintner Plotkin & Kahn, PLLC

King L. Wong

King L. Wong
Attorney for Applicant(s)
Registration No. 37,500

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1050 Connecticut Avenue, N.W., Suite 600
Washington, D.C. 20036-5339
Tel.: (202) 857-6000
Fax: (202) 638-4810

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